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     (FILE 'HOME' ENTERED AT 09:20:20 ON 14 APR 2005)

     FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 09:20:39 ON 14 APR 2005
L1        285290 S INTERFERON
L2         90153 S CHIMERIC
L3          1012 S L1 (L) L2
L4       1684344 S ANTIBODY
L5         86665 S FC
L6         22529 S L4 (L) L5
L7            31 S L3 (L) L6
L8            16 DUP REM L7 (15 DUPLICATES REMOVED)
L9        288715 S HYBRID
L10       374011 S L9 OR L2
L11         3163 S L1 (L) L10
L12           49 S L11 AND L6
L13           30 DUP REM L12 (19 DUPLICATES REMOVED)
L14           17 S L13 AND PY<2001
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L14 ANSWER 1 OF 17 MEDLINE on STN
TI Effects of a **hybrid** recombinant human alpha **interferon** (A/D) on in vitro cytotoxicity and in vivo localization of monoclonal antibody L6-cytosine deaminase conjugate in a colon cancer model.
PY 1998
SO Cancer biotherapy & radiopharmaceuticals, **(1998 Feb)** 13 (1) 33-42.
Journal code: 9605408. ISSN: 1084-9785.
TI Effects of a **hybrid** recombinant human alpha **interferon** (A/D) on in vitro cytotoxicity and in vivo localization of monoclonal antibody L6-cytosine deaminase conjugate in a colon cancer model.. . .
SO Cancer biotherapy & radiopharmaceuticals, **(1998 Feb)** 13 (1) 33-42.
Journal code: 9605408. ISSN: 1084-9785.
AB L6 is an IgG2a murine monoclonal **antibody** which we have demonstrated binds well to HT29 human colon carcinoma cells by flow cytometry, whole cell ELISA, and mixed hemadsorption. In vitro cytotoxicity studies revealed that the monoclonal **antibody** L6-cytosine deaminase (L6-CD) immunoconjugate plus the nontoxic prodrug, 5-fluorocytosine (5-**FC**), is equivalent to 5-fluorouracil (5-FU) in its ability to kill HT29 cells. Human alpha-interferon (A/D) was able to enhance this. . . are needed for this cytotoxic effect (approximately, 5 pg/ml resulted in 50% viability). The limiting factor was the amount of 5-**FC** employed with L6-CD (3 microM yielded 50% cell viability). alpha-Interferon (A/D) lowered the requirement of 5-**FC** to 1 microM to achieve 50% cell lethality. In vivo biodistribution experiments indicated that 1 microgram of L6-CD is nonspecifically. . . in percent injected dose per gram of tumor was possible with the intravenous injection of 100 micrograms of anti-idiotypic monoclonal **antibody** 13B, 24 hours after L6-CD, which bound unreacted L6-CD and cleared it from the blood. The addition of 100,000 U. . .

L14 ANSWER 2 OF 17 MEDLINE on STN
TI CD4+ T-cell-mediated cytotoxicity against staphylococcal enterotoxin B-pulsed synovial cells.
PY 1998
SO Immunology, **(1998 Sep)** 95 (1) 38-46.
Journal code: 0374672. ISSN: 0019-2805.
SO Immunology, **(1998 Sep)** 95 (1) 38-46.
Journal code: 0374672. ISSN: 0019-2805.
AB . . . synovial cells in a staphylococcal enterotoxin B (SEB)-dependent manner, inducing synovial cell apoptosis. Synovial cells were cultured with or without **interferon**-gamma (IFN-gamma) and further incubated with CD4+ T cells in the presence of SEB. After the cocultivation, both the cytotoxicity and. . . was markedly induced, significant cytotoxicity by these cells against synovial cells was detected. The addition of anti-HLA-DR and -DQ monoclonal **antibodies** (mAbs) or human Fas **chimeric** protein (hFas-**Fc**) reduced this cytotoxicity. FasL expression of CD4+ T cells cocultured with IFN-gamma-stimulated synovial cells with SEB was significantly induced. Furthermore,. . .

L14 ANSWER 3 OF 17 MEDLINE on STN
TI Fas/Fas ligand interaction regulates cytotoxicity of CD4+ T cells against staphylococcal enterotoxin B-pulsed endothelial cells.
PY 1997
SO Biochemical and biophysical research communications, **(1997 Oct 29)** 239 (3) 782-8.
Journal code: 0372516. ISSN: 0006-291X.
SO Biochemical and biophysical research communications, **(1997 Oct 29)** 239 (3) 782-8.
Journal code: 0372516. ISSN: 0006-291X.
AB . . . by endothelial cells, in inducing endothelial cell apoptosis. The human endothelial cell line, EA.hy926 cells, was cultured with or without **interferon**-gamma (IFN-gamma) and further incubated with CD4+ T cells in the presence or absence of SEB. After this cocultivation,

the cytotoxicity. . . EA.hy926 cells with augmented HLA-DR and -DQ expression, this cytotoxicity was more significant. The addition of anti-HLA-DR and -DQ monoclonal **antibodies** (mAbs) or human Fas **chimeric** protein (hFas-**Fc**) reduced the cytotoxicity. FasL expression was induced in CD4+ T cells cocultured with SEB-pulsed EA.hy926 cells, especially when the EA.hy926. . .

L14 ANSWER 4 OF 17 MEDLINE on STN
TI Intercellular adhesion molecule-3 is the predominant co-stimulatory ligand for leukocyte function antigen-1 on human blood dendritic cells.
PY 1995
SO European journal of immunology, **(1995 Sep)** 25 (9) 2528-32. Journal code: 1273201. ISSN: 0014-2980.
SO European journal of immunology, **(1995 Sep)** 25 (9) 2528-32. Journal code: 1273201. ISSN: 0014-2980.
AB . . . the DC. Although blood and tonsil DC express ICAM-1 (CD54) and ICAM-2 (CD102) on their surface, anti-ICAM-1 and anti-ICAM-2 monoclonal **antibodies** (mAb) have little inhibitory activity on the DC-stimulated mixed leukocyte reaction (MLR). We therefore examined the expression of the more. . . blood DC expressed significantly more ICAM-3 than ICAM-1 or ICAM-2 as assessed by flow cytometry. Treatment of resting DC with **interferon**-gamma led to increased expression of ICAM-1; however, ICAM-2 and ICAM-3 levels remained relatively constant. Solid-phase recombinant **chimeric** molecules ICAM-1-, ICAM-2- and ICAM-3-**Fc** were able to co-stimulate CD4+ T lymphocyte proliferation in conjunction with suboptimal solid-phase CD3 mAb 64.1. However, the anti-ICAM-3 mAb. . .

L14 ANSWER 5 OF 17 MEDLINE on STN
TI The extended hinge region of IgG3 is not required for high phagocytic capacity mediated by Fc gamma receptors, but the heavy chains must be disulfide bonded.
PY 1993
SO European journal of immunology, **(1993 Jul)** 23 (7) 1546-51. Journal code: 1273201. ISSN: 0014-2980.
SO European journal of immunology, **(1993 Jul)** 23 (7) 1546-51. Journal code: 1273201. ISSN: 0014-2980.
AB **Fc** gamma receptor (**Fc** gamma R) phagocytosis and respiratory burst were induced by **chimeric** mouse-human anti-(4-hydroxy-5-iodo-3-nitrophenyl) acetyl IgG3 **antibodies** with mutations in hinge and/or in CH1 region. IgG3 mutants with different hinge length ranging from 47 to 0 amino acids, an IgG3 molecule with an artificial hinge of just one cysteine residue (HM-1), and two **hybrid** IgG3 molecules with IgG4 hinge or IgG4 CH1-hinge were tested. Using the monocytic cell line U937 as effector cells, the mutated IgG3 molecules were very similar, revealing high activity, while the IgG3/IgG4 **hybrids** revealed a slightly reduced activity. However, the hingeless (0-h) mutant was negative, except after **interferon**-gamma stimulation when it became slightly positive. Interestingly, HM-1 was as active as the IgG3 mutants. With polymorphonuclear leucocytes (PMN) as. . . variations, but all the IgG3 mutants were highly active, with the two shortest hinge mutants somewhat less active. The IgG3/IgG4 **hybrid** molecules revealed an intermediate activity, while IgG4 wild-type and the 0-h mutant were negative. However, the HM-1 molecule revealed an. . . to that of the IgG3 mutants. The phagocytic activity of U937 was inhibited by monomeric IgG, indicating the importance of **Fc** gamma RI. In contrast, with PMN both blockage of **Fc** gamma RII and cleavage of **Fc** gamma RIII were required to significantly reduce the phagocytosis and respiratory burst, thus showing that both receptors contribute to the. . .

L14 ANSWER 6 OF 17 MEDLINE on STN
TI Augmentation of tumor antigen expression by recombinant human interferons: enhanced targeting of monoclonal antibodies to carcinomas.
PY 1990
SO Cancer treatment and research, **(1990)** 51 413-32. Ref: 59 Journal code: 8008541. ISSN: 0927-3042.

SO Cancer treatment and research, **(1990)** 51 413-32. Ref: 59
Journal code: 8008541. ISSN: 0927-3042.

AB . . . standpoint, studies using the intact IgG have shown that, in a majority of patients injected with IgG, human anti-mouse IgG **antibodies** develop that hamper the effectiveness of subsequent **antibody** administration. It is believed that the human anti-mouse **antibody** response is directed against the **Fc** region of the IgG molecule. The elimination of this region through fractionation of the Mab to obtain the minimum binding. . . the genes encoding for individual Mabs, reduce them via restriction endonuclease techniques, and insert human immunoglobulin constant regions. The resulting **chimeric antibodies** are believed to reduce the development of human anti-mouse **antibodies**. Effective Mab therapy of human tumor lesions may also be achieved through the recruitment of a portion of the host's. . . An example is the use of anti-idiotype Mabs that use as immunogen a Mab to a tumor antigen. The anti-idiotype **antibodies** are selected for binding to the antigen binding, or idiotype, region of the first Mab. The binding sites of the new anti-idiotype Mabs should reflect the 'internal image' of the original antigen. The anti-idiotype **antibodies** may be used to immunize patients (i.e., vaccines) in an attempt to mount an active immune response against the antigen-positive tumor cells. Recent studies have shown a synergism between **interferon**-alpha and an anti-idiotype Mab for the in-vivo antitumor activity in a murine B-cell lymphoma experimental model. Whether an **interferon**-mediated increase in the tumor antigen or the **Fc** receptor was part of the synergism was not investigated. Mabs alone have also been shown to elicit cytotoxic activity in vitro and tumoricidal activity in vivo. **Antibodies** of the IgG2a isotype can direct macrophage-mediated cytotoxicity. These studies revealed the importance of the number of **antibody** sites per cell as well as the number of cells that bind the IgG2a Mab, thus suggesting a 'threshold' requirement. . .

L14 ANSWER 7 OF 17 MEDLINE on STN

TI Interferon-alpha A/D blocks an increase in Fc receptors of a human promyelocytic leukemia cell line (HL-60) induced by other recombinant interferons.

PY 1987

SO Journal of interferon research, **(1987 Aug)** 7 (4) 397-407.
Journal code: 8100396. ISSN: 0197-8357.

SO Journal of interferon research, **(1987 Aug)** 7 (4) 397-407.
Journal code: 8100396. ISSN: 0197-8357.

AB The effect of recombinant **hybrid interferon** (IFN)-alpha A/D either alone or in combination with retinoic acid (RA) on induction of differentiation of the human promyelocytic leukemia. . . units/ml and higher induces differentiation into cells having many monocytic characteristics such as monocyte-like morphology, ability of superoxide anion production, **antibody**-dependent cellular cytotoxicity, and nonspecific esterase activity. However, this combination does not induce an increase in IgG **Fc** receptors (**Fc** gamma R) and immunoerythrophagocytosis. IFN-alpha A/D alone shows essentially no effect on these parameters. Pretreatment of HL-60 with IFN-alpha A/D blocks the **Fc** gamma R-increasing activity of IFN-alpha A, IFN-alpha D, and IFN-gamma. This block is complete after a 2-h pretreatment for IFN-alpha A and IFN-alpha D and after a 6-h pretreatment for IFN-gamma. Furthermore, an increase in **Fc** gamma R-mediated phagocytosis is also suppressed by the pretreatment. However, IFN-alpha A/D does not suppress superoxide anion production. These results indicate that the block of an **Fc** gamma R-increase by IFN-alpha A/D has not resulted in the competitive inhibition at IFN receptors, but may occur in intracellular events such as postreceptor transduction for the expression of **Fc** gamma R.

L14 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

TI Functional balance between T cell chimeric receptor density and tumor associated antigen density: CTL mediated cytolysis and lymphokine production

PY **2000**

SO Gene Therapy (**2000**), 7(1), 35-42
CODEN: GETHEC; ISSN: 0969-7128
SO Gene Therapy (**2000**), 7(1), 35-42
CODEN: GETHEC; ISSN: 0969-7128
AB Genetically engineered expression of tumor-specific single chain **antibody** chimeric receptors (ch-Rec) on human T lymphocytes endow these cells with the parental monoclonal **antibody** (mAb) dictated tumor specificity and may be useful for clin. immuno-gene therapy. Therefore it was of importance to assess how. . . a ch-Rec derived from (1) a renal carcinoma cell (RCC) specific mouse mAb (G250), and (2) the human signal transducing **Fc**(ε)RI γ-chain was used. To obtain ch-RecHIGH-POS and ch-RecLOW-POS T lymphocytes, two distinct retroviral vectors were used to introduce the gene. . .
IT **Antibodies**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(single chain, TAA-specific, fusion protein with **Fc** εRI γ-chain; functional balance between T cell chimeric receptor d. and tumor associated antigen d. in relation to CTL mediated cytolysis and lymphokine production)
IT **Interferons**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(γ; functional balance between T cell **chimeric** receptor d. and tumor associated antigen d. in relation to CTL mediated cytolysis and lymphokine production)

L14 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Specific targeting of EGP-2+ tumor cells by primary lymphocytes modified with chimeric T cell receptors
PY **2000**
SO Human Gene Therapy (**2000**), 11(1), 9-19
CODEN: HGTHE3; ISSN: 1043-0342
SO Human Gene Therapy (**2000**), 11(1), 9-19
CODEN: HGTHE3; ISSN: 1043-0342
AB . . . two novel cTCR mols. (GAγ and GAHγ) were investigated. Both encode a single-chain variable fragment (scFv) derived from the monoclonal **antibody** (MAb) GA733.2, which binds the epithelial glycoprotein 2 (EGP-2) overexpressed on a variety of human carcinomas. In the GAγ cTCR, the scFv is directly fused to the transmembrane/cytoplasmic portions of the Ig **Fc** receptor (Ig FcRI) γ subunit, which mediates T cell signaling. GAHγ possesses an extracellular spacer composed of the CD8α Ig. . .
IT **Interferons**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(γ; specific targeting of EGP-2+ tumor cells by primary lymphocytes modified with **chimeric** T cell receptors and formation of)

L14 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Binding agents for treatment of inflammatory, autoimmune or allergic diseases
PY 1996
1996
1996
1996
1999
1997
1998
1998
1998
1998
1998
2000
2000

2001
2001
2001
1996
1999

SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2

PI WO 9612742 A1 **19960502**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9612742	A1	19960502	WO 1995-EP4110	19951020 <--
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2203363	AA	19960502	CA 1995-2203363	19951020 <--
CA 2203364	AA	19960502	CA 1995-2203364	19951020 <--
AU 9538679	A1	19960515	AU 1995-38679	19951020 <--
AU 710369	B2	19990916		
EP 788514	A1	19970813	EP 1995-937803	19951020 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509434	A	19980106	BR 1995-9434	19951020 <--
CN 1169735	A	19980107	CN 1995-196799	19951020 <--
CN 1171119	A	19980121	CN 1995-197075	19951020 <--
HU 77572	A2	19980629	HU 1998-339	19951020 <--
JP 10507460	T2	19980721	JP 1995-513642	19951020 <--
EP 1018517	A2	20000712	EP 1999-204301	19951020 <--
EP 1018517	A3	20000726		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
ES 2154741	T3	20010416	ES 1995-936525	19951020
PT 788513	T	20010629	PT 1995-936525	19951020
JP 2001316291	A2	20011113	JP 2001-127383	19951020
ZA 9508947	A	19960731	ZA 1995-8947	19951023 <--
IL 115733	A1	19991222	IL 1995-115733	19951024 <--

IT Immunoglobulin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**Fc**εRII (IgE fragment **Fc** receptor II), humanized or chimeric **antibody** and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Interferons**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α, humanized or **chimeric** antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

L14 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Expression and characterization of a divalent chimeric anti-human CD3 single chain antibody
PY **1996**
SO Scandinavian Journal of Immunology (**1996**), 43(2), 134-9
CODEN: SJIMAX; ISSN: 0300-9475
SO Scandinavian Journal of Immunology (**1996**), 43(2), 134-9
CODEN: SJIMAX; ISSN: 0300-9475
AB Murine anti-CD3 monoclonal **antibodies** (MoAbs) are used in clin. practice for immunosuppression. However, there are two major drawbacks to this treatment: the associated cytokine release syndrome and human anti-mouse **antibody** response. To overcome these side-effects, the authors generated a chimeric anti-human CD3 single chain **antibody**, scUCHT1. It is an IgM variant of UCHT1, a mouse IgG1 MoAb directed against human CD3. ScUCHT1 consists of the light and heavy variable chain binding domains of UCHT1 and a human IgM **Fc** region (CH2 to CH4).

ScUCHT1 was produced by COS-7 and SP2/0 transfectants, and mainly assembled in a dimeric form. It. . . and cytokine release (TNF-α and IFN-γ) in in vitro assays. These results suggest that the engineered chimeric anti-CD3 single chain **antibody** (scUCHT1) may be useful in clin. immunosuppressive treatment.

IT **Interferons**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(γ, effect of divalent **chimeric** anti-CD3 single chain antibody on cytokine formation)

L14 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Colony-stimulating factor enhancement of myeloid effector cell cytotoxicity towards neuroectodermal tumor cells
PY **1993**
SO British Journal of Haematology (**1993**), 83(4), 545-63
CODEN: BJHEAL; ISSN: 0007-1048
SO British Journal of Haematology (**1993**), 83(4), 545-63
CODEN: BJHEAL; ISSN: 0007-1048
AB Expts. were conducted to determine the optimal conditions for colony-stimulating factor-enhanced neutrophil- and mononuclear phagocyte-mediated **antibody**-dependent cell-mediated cytotoxicity (ADCC) using monoclonal **antibodies** to disialogangliosides expressed on neuroectodermal tumor target cells. Neutrophil ADCC was most effective at effector:target ratios of 100:1, with maximal. . . factor (G-CSF) were the most potent stimulators of neutrophil ADCC, and enhanced ADCC activity was inhibited in the presence of **antibody** to **Fc** receptor type II (FcRII). GM-CSF and macrophage colony-stimulating factor (M-CSF) treatment of freshly isolated monocytes inhibited **antibody**-independent cytotoxicity but enhanced **antibody**-dependent responses. After 3 days in culture with CSF, 3-10-fold enhancement of ADCC against melanoma target cells was observed at effector:target. . . ADCC was obtained when GM-CSF, M-CSF, or interleukin 3 (IL-3) were used in conjunction with a secondary stimulus. Although γ **interferon** (γ-IFN) did not augment the cytotoxic capability of GM-CSF- and IL-3-stimulated macrophages, prominent cytotoxic enhancement was seen when M-CSF-stimulated macrophages were exposed to γ-IFN. A **chimeric** mouse/human monoclonal **antibody** was found to be equivalent in activity to the murine **antibody** in neutrophil ADCC; however, in macrophage ADCC assays with submaximal effector cell stimulation, the **chimeric** **antibody** was associated with a 2-fold greater response. Thus, under specific conditions, CSFs capable of increasing the number and functional activity of mature myeloid effector cells enhance **antibody** -dependent cytotoxicity to neuroectodermal tumor target cells.

L14 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Mapping and comparison of the interaction sites on the **Fc** region of IgG responsible for triggering **antibody** dependent cellular cytotoxicity (ADCC) through different types of human **Fcγ** receptor
PY **1992**
SO Molecular Immunology (**1992**), 29(5), 633-9
CODEN: MOIMD5; ISSN: 0161-5890
TI Mapping and comparison of the interaction sites on the **Fc** region of IgG responsible for triggering **antibody** dependent cellular cytotoxicity (ADCC) through different types of human **Fcγ** receptor
SO Molecular Immunology (**1992**), 29(5), 633-9
CODEN: MOIMD5; ISSN: 0161-5890
AB In the present study 3-iodo-4-hydroxy-5-nitrophenacetyl (NIP)-specific **antibodies** were compared for induction of **antibody** dependent lysis (ADCC) of NIP-derivatized red blood cells effected by pre-stimulated U937 or HL-60 cells and by killer (K) cells. **Chimeric antibodies** were used having heavy chains corresponding to human IgG subclasses 1-4, and including site-directed mutants of IgG3 as well as the aglycosylated form of IgG3; a mouse IgG2b **antibody** and a site-directed mutant IgG2b were also examined

Recombinant **interferon** (rIFN)-stimulated U937 or HL-60 cells express increased levels of **Fc**γRI compared to unstimulated cells; PMA stimulated HL-60 and U937 cells to express an increased level of **Fc**γRII compared to unstimulated cells; K cells expressed **Fc**γRIII. Using these effector cell populations and the target cells mentioned above, anti-NIP **antibodies** were compared with different heavy chain constant domains for their ability to induce ADCC through human **Fc**γRI, **Fc**γRII and **Fc**γRIII. The results suggest that all three human **Fc**γ receptors appear to recognize a binding site on IgG within the lower hinge (residues 234-237) and trigger ADCC via this. . .

IT Cytolysis
(**antibody**-dependent cell-mediated, of humans, **Fc** γ receptors interaction site on ligand in)

IT Monocyte
(**antibody**-dependent cytolysis by human, **Fc**γ receptors interaction site on ligand in)

IT Leukocyte
(granulocyte, **antibody**-dependent cytolysis by human, **Fc**γ receptors interaction site on ligand in)

IT Lymphocyte
(killer cell, **antibody**-dependent cytolysis by human, **Fc**γ receptors interaction site on ligand in)

L14 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

TI Multivalent anti-cytokine immunoglobulins

PY 1992
1992
1993
1994
1993
1993
1994

SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2

PI WO 9201472 A1 **19920206**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9201472	A1	19920206	WO 1991-GB1216	19910719 <--
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MN, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9182381	A1	19920218	AU 1991-82381	19910719 <--
EP 539455	A1	19930505	EP 1991-913265	19910719 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06501840	T2	19940303	JP 1991-512563	19910719 <--
NO 9300153	A	19930316	NO 1993-153	19930118 <--
GB 2261666	A1	19930526	GB 1993-960	19930119 <--
GB 2261666	B2	19940727		

AB Multivalent Igs comprising ≥3 linked antigen-binding domains specific for a site on a cytokine [e.g. tumor necrosis factors (TNFs), interleukins, **interferons**, colony-stimulating factors] are prepared that have increased neutralizing activity and are useful for therapeutic or prophylactic treatment of conditions involving. . . class. The Igs may comprise recombinant Igs and fragments, and the antigen-binding domains may be covalently or noncovalently linked. Recombinant **chimeric** IgM anti-TNF-α antibodies were prepared by ligating DNA coding for the light and heavy chain variable domains of the murine. . . constant region and human μ heavy chain constant region, resp. COS cells were transfected with the gene coding for the **chimeric** light chain together with plasmid pE2058, pE2059, pE2060, or pE2061 carrying a **chimeric** heavy chain gene. Lower amts. of the recombinant **chimeric** IgM product than the murine 101.4 IgG were required for neutralization of TNF-α.

IT **Antibodies**
RL: BIOL (Biological study)
(to **Fc** region of IgG, anti-tumor necrosis factor-α IgGs

crosslinked with, TNF-α-neutralizing activity of)

L14 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Anti-Rh(D) heteroantibodies and pharmaceutical composition containing same for drug targeting and therapy using macrophages
PY 1991
1991
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
PI WO 9105800 A1 **19910502**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9105800	A1	19910502	WO 1990-FR757	19901019 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
FR 2653561	A1	19910426	FR 1989-13678	19891019 <--

AB **Chimeric antibodies** comprise all or part of anti-Rh(D) blood-group substance **antibody** linked with all or part of an **antibody** to a receptor for **Fc** fragment of Igs that is not blocked by IgG. These **chimeric antibodies** are bound to erythrocytes encapsulating, e.g. macrophage activators, antiinfective agents, and anticancer agents, via the Rh(D) surface antigen on the erythrocytes, and the complexes target macrophages and are thus useful in therapies involving macrophages. The F(ab')2 fragment of monoclonal **antibody** H2D5D2 (anti D) was coupled to the FAb' fragment of monoclonal **antibody** 32.2 (anti **Fc** γRI). This **chimeric antibody** was reacted with Rh-pos. erythrocytes loaded with γ **interferon**. U937 tumor cells were inhibited using human macrophages and the complex.

IT Immunoglobulins
RL: BIOL (Biological study)
(**Fc** fragment of, receptors for, bispecific **antibody** to Rh(D) blood-group substance and to)

IT Receptors
RL: BIOL (Biological study)
(**Fc**γRI, bispecific **antibody** to Rh(D) blood-group substance and to)

IT **Antibodies**
RL: BIOL (Biological study)
(bispecific, to Rh(D) blood-group substances and to receptor for **Fc** fragment of Igs)

IT Erythrocyte
(drug-loaded, complex with bispecific **antibody** to erythrocyte surface antigen and to receptor for **Fc** fragment of Igs, for macrophage targeting and therapy)

IT Anti-infective agents
Antibiotics
Immunostimulants
Neoplasm inhibitors
Parasiticides
Virucides and Virustats
(erythrocyte-encapsulated, bispecific **antibody** to erythrocyte surface antigen and to receptor for **Fc** fragment of Igs complex with, for macrophage targeting and therapy)

IT Receptors
RL: BIOL (Biological study)
(for fragment **Fc** of Igs, bispecific **antibody** to Rh(D) blood-group substance and to)

IT Pharmaceutical dosage forms
(of drug-loaded erythrocyte complexes with bispecific **antibody** to erythrocyte surface antigen and to Ig **Fc** fragment receptor, for macrophage targeting and therapy)

IT Encapsulation
(of interferon γ in erythrocytes complexed with bispecific **antibody** to Rh(D) blood-group substance and to **Fc** γRI receptors)

IT Immunoglobulins
RL: BIOL (Biological study)

(G, receptor for **Fc** fragment of Igs not blocked by, bispecific **antibody** to Rh(D) blood-group substance and to)

IT Blood-group substances
RL: BIOL (Biological study)
(Rh(D), bispecific **antibody** to receptor for **Fc** fragment of Igs and to)

IT Pharmaceutical dosage forms
(injections, of drug-loaded erythrocyte complexes with bispecific **antibody** to erythrocyte surface antigen and to Ig **Fc** fragment receptor, for macrophage targeting and therapy)

IT Fungicides and Fungistats
(medical, erythrocyte-encapsulated, bispecific **antibody** to erythrocyte surface antigen and to receptor for **Fc** fragment of Igs complex with, for macrophage targeting and therapy)

IT Antigens
RL: BIOL (Biological study)
(surface, of erythrocytes, bispecific **antibody** to receptor for **Fc** fragment of Igs and to)

IT Interferons
RL: BIOL (Biological study)
(γ, erythrocyte-encapsulated, bispecific **antibody** to Rh(D) blood-group substance and to **Fc**γRI receptors complexed with, macrophage targeting and neoplasm inhibition with)

L14 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synergistic antitumor activity with IFN and monoclonal antiidiotype for murine B cell lymphoma. Mechanism of action
PY **1988**
SO Journal of Immunology (**1988**), 141(8), 2855-60
CODEN: JOIMA3; ISSN: 0022-1767
SO Journal of Immunology (**1988**), 141(8), 2855-60
CODEN: JOIMA3; ISSN: 0022-1767
AB Combination therapy with syngeneic anti-idiotype **antibody** and human **hybrid** recombinant **interferon**-α (rIFN-α) A/D synergistically increase survival in C3H/HeN mice challenged with a LD of tumor cells. C3H/HeJ mice, which have previously been described to be LPS hyporesponsive and have a defect in **Fc** γR (receptor) function, did not respond to anti-idiotype therapy as well as C3H/HeN normal mice. This defect was completely corrected in. . . into F(ab')2 fragments no longer had any antitumor activity alone and could not be enhanced by IFN therapy. Apparently, the **antibody** is functioning through **Fc**γR-bearing effector cells that are enhanced by IFN therapy. Synergy between IFN and anti-idiotype mAb was maintained in nude mice lacking. . .

L14 ANSWER 17 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Phase I study of interleukin-12 in combination with rituximab in patients with B-cell non-Hodgkin's lymphoma (NHL).
PY **2000**
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 577a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 577a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
AB Rituximab is a genetically engineered **chimeric** murine/human monoclonal **antibody** that binds specifically to CD20 on pre-B and mature B-lymphocytes. While binding of the Fab domain may induce apoptosis, the **Fc** domain recruits immune effector functions to mediate lysis of the B-cell. Interleukin-12 (IL-12) has been shown to facilitate cytolytic T-cell. . . responses, promote the development of Th1-type helper T-cells, enhance the lytic activity of NK cells, and induce the secretion of **interferon**-gamma by both T and NK cells.

Therefore, we hypothesized that combining IL-12 with Rituximab would augment the immune mediated cell. . . and liver enzyme elevations were found to be dose limiting. A >100% increase from baseline in the serum levels of **interferon**-gamma and Inducible Protein-10 (IP-10) in response to IL-12 were seen at IL-12 doses of 100ng/kg, 300ng/kg and 500ng/kg. Significant constitutional. . .

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=> d his

     (FILE 'HOME' ENTERED AT 09:20:20 ON 14 APR 2005)

     FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 09:20:39 ON 14 APR 2005
L1        285290 S INTERFERON
L2         90153 S CHIMERIC
L3          1012 S L1 (L) L2
L4       1684344 S ANTIBODY
L5         86665 S FC
L6         22529 S L4 (L) L5
L7            31 S L3 (L) L6
L8            16 DUP REM L7 (15 DUPLICATES REMOVED)
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=> s interferon
L1      285290 INTERFERON

=> s chimeric
L2       90153 CHIMERIC

=> s l1 (l) l2
L3        1012 L1 (L) L2

=> s antibody
L4     1684344 ANTIBODY

=> s Fc
L5       86665 FC

=> s l4 (l) l5
L6       22529 L4 (L) L5

=> s l3 (l) l6
L7          31 L3 (L) L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           16 DUP REM L7 (15 DUPLICATES REMOVED)

=> d l8 1-16 ti py so kwic

L8   ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   Fusion proteins of interferon alpha (INFα), particularly,
     INFα2 muteins with Fc domain of a human antibody, and uses against
     hepatitis C virus
PY   2004
SO   PCT Int. Appl., 54 pp.
     CODEN: PIXXD2
IT   Fusion proteins (chimeric proteins)
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (Fc-INFα2; fusion proteins of  interferon
        alpha (INFα), particularly, INFα2 muteins with   Fc
        domain of human antibody, and uses against hepatitis C virus)

L8   ANSWER 2 OF 16  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   Interferon β and human IgG1 Fc chimeric proteins for treating
     glomerulonephritis and chronic renal failure
PY   2004
     2004
SO   PCT Int. Appl., 90 pp.
     CODEN: PIXXD2
IT   Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (IgG1, Fc; interferon β and human IgG1
        Fc chimeric proteins for treating glomerulonephritis
        and chronic renal failure)
IT   Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (fragments, Fc; interferon β and human IgG1
        Fc chimeric proteins for treating glomerulonephritis
        and chronic renal failure)
IT   Antibodies and Immunoglobulins
     RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (heavy chain, chimeric interferon β;
```

interferon β and human IgG1 **Fc chimeric** proteins for treating glomerulonephritis and chronic renal failure)

L8 ANSWER 3 OF 16 MEDLINE on STN DUPLICATE 1
TI Specific regulation of T helper cell 1-mediated murine colitis by CEACAM1.
PY 2004
SO Journal of experimental medicine, (2004 Feb 16) 199 (4) 471-82.
Journal code: 2985109R. ISSN: 0022-1007.
AB . . . T helper cell (Th)1 pathways, T-bet-mediated Th1 cytokine signaling, and Th1-mediated immunopathology in vivo. Mice treated with anti-mouse CEACAM1-specific monoclonal **antibody** (mAb) CC1 during the effector phase exhibited a reduced severity of trinitrobenzene sulfonic acid colitis in association with decreased **interferon** (IFN)-gamma production. Although oxazolone colitis has been reported as Th2 mediated, mice treated with the CC1 mAb or a CEACAM1-**Fc chimeric** protein exhibited a reduced severity of colitis in association with a significant reduction of IFN-gamma and T-bet activation, whereas signal. . .

L8 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 2
TI Adding cytokines to monoclonal antibody therapy: does the concurrent administration of interleukin-12 add to the efficacy of rituximab in B-cell non-hodgkin lymphoma?.
PY 2003
SO Leukemia & lymphoma, (2003 Aug) 44 (8) 1309-15. Ref: 46
Journal code: 9007422. ISSN: 1042-8194.
AB . . . is a cytokine that facilitates cytolytic T-cell responses, enhances the lytic activity of NK cells and induces the secretion of **interferon**-gamma by both T and NK cells. Binding of rituximab, a **chimeric** murine/human monoclonal **antibody**, to CD20 on B-lymphocytes induces apoptosis and the **Fc** domain of the **antibody** recruits immune effector functions to mediate cell lysis. Therefore, combining IL-12 with rituximab in patients with B-cell non-Hodgkin lymphoma (NHL). . . of the combination. The two agents, when given in combination, significantly upregulate the patient's immune mechanisms. The combination upregulates gamma **interferon** and IP-10 expression and increases NK cell lytic activity. The combination appears to have significant clinical activity with a high. . .

L8 ANSWER 5 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI In vitro and in vivo antitumor activity of a mouse CTL hybridoma expressing chimeric receptors bearing the single chain Fv from HER-2/neu-specific antibody and the gamma-chain from Fc(epsilon) RI.
PY 2003
SO Cancer Immunology Immunotherapy, (August 2003) Vol. 52, No. 8, pp. 513-522. print.
CODEN: CIIMDN. ISSN: 0340-7004.
IT . . .
neoplastic disease, immunology, therapy
Neoplasms (MeSH)
IT Diseases
severe combined immunodeficiency: immune system disease
Severe Combined Immunodeficiency (MeSH)
IT Chemicals & Biochemicals
Fc(epsilon) RI gamma-chain; HER-2/neu: overexpression; HER-2/neu-specific **antibody** single chain Fv; IFN-gamma [**interferon**-gamma]: secretion; IL-2 [interleukin-2]: secretion; **chimeric** receptors; scFv(anti-HER-2/neu)/gamma **chimeric** protein: expression

L8 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 3
TI Phase 1 study of interleukin-12 in combination with rituximab in patients with B-cell non-Hodgkin lymphoma.
PY 2002
SO Blood, (2002 Jan 1) 99 (1) 67-74.
Journal code: 7603509. ISSN: 0006-4971.
AB Rituximab is a **chimeric** murine/human monoclonal **antibody** that binds to CD20 on B lymphocytes. Although binding of the Fab domain

may induce apoptosis, the **Fc** domain recruits immune effector functions to mediate cell lysis. Interleukin-12 (IL-12) facilitates cytolytic T-cell responses, enhances the lytic activity of natural killer (NK) cells, and induces the secretion of **interferon** gamma (IFN-gamma) by both T and NK cells. Therefore, the hypothesis was considered that combining IL-12 with rituximab would augment. . .

L8 ANSWER 7 OF 16 MEDLINE on STN DUPLICATE 4
TI Monoclonal antibodies in the treatment of malignancy: basic concepts and recent developments.
PY 2001
SO Cancer investigation, (2001) 19 (8) 833-41. Ref: 75
Journal code: 8307154. ISSN: 0735-7907.
AB **Antibodies** have long been considered to be potential anticancer agents because of their specificity for cell-membrane antigens. Applications of hybridoma and recombinant DNA technology have led to the production of unlimited quantities of clinical-grade murine, **chimeric**, and humanized monoclonal **antibodies** for clinical use. Whole **antibodies** may produce anticancer effects in conjunction with the immune system by interaction with complement proteins and/or effector cells via the **Fc** portion of the **antibody** molecule. **Antibodies** may also neutralize circulating ligands or block cell membrane receptors and thus interrupt ligand/receptor interactions and signal transduction that are associated with proliferative or anti-apoptotic effects. The anti-idiotype network cascade provides a rationale for **antibodies** as vaccine therapy. **Antibodies** may also serve as the guiding or targeting system for other cytotoxic pharmaceutical products such as (i) radiolabeled **antibodies** for radioimmunodetection and radioimmunotherapy; (ii) immunotoxins; (iii) chemotherapy/**antibody** conjugates; (iv) cytokine/**antibody** conjugates; and (v) immune cell/**antibody** conjugates. After years of anticipation, as of late 1999 there were four monoclonal **antibodies** that had been approved by the U.S. Food and Drug Administration based on activity against human malignancy, all of which are in widespread clinical use. Several other products are in various stages of clinical trial testing. Monoclonal **antibodies** have joined **interferon**-alpha, interleukin-2 (IL-2), and various hematopoietic growth factors as well-established components of biological therapy, the fourth modality of cancer treatment.

L8 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Phase I study of interleukin-12 in combination with rituximab in patients with B-cell non-Hodgkin's lymphoma (NHL).
PY 2000
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 577a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
AB Rituximab is a genetically engineered **chimeric** murine/human monoclonal **antibody** that binds specifically to CD20 on pre-B and mature B-lymphocytes. While binding of the Fab domain may induce apoptosis, the **Fc** domain recruits immune effector functions to mediate lysis of the B-cell. Interleukin-12 (IL-12) has been shown to facilitate cytolytic T-cell. . . responses, promote the development of Th1-type helper T-cells, enhance the lytic activity of NK cells, and induce the secretion of **interferon**-gamma by both T and NK cells. Therefore, we hypothesized that combining IL-12 with Rituximab would augment the immune mediated cell. . . and liver enzyme elevations were found to be dose limiting. A >100% increase from baseline in the serum levels of **interferon**-gamma and Inducible Protein-10 (IP-10) in response to IL-12 were seen at IL-12 doses of 100ng/kg, 300ng/kg and 500ng/kg. Significant constitutional. . .

L8 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 5
TI CD4+ T-cell-mediated cytotoxicity against staphylococcal enterotoxin B-pulsed synovial cells.
PY 1998

SO . Immunology, (1998 Sep) 95 (1) 38-46.
Journal code: 0374672. ISSN: 0019-2805.
AB . . . synovial cells in a staphylococcal enterotoxin B (SEB)-dependent manner, inducing synovial cell apoptosis. Synovial cells were cultured with or without **interferon**-gamma (IFN-gamma) and further incubated with CD4+ T cells in the presence of SEB. After the cocultivation, both the cytotoxicity and. . . was markedly induced, significant cytotoxicity by these cells against synovial cells was detected. The addition of anti-HLA-DR and -DQ monoclonal **antibodies** (mAbs) or human Fas **chimeric** protein (hFas-**Fc**) reduced this cytotoxicity. FasL expression of CD4+ T cells cocultured with IFN-gamma-stimulated synovial cells with SEB was significantly induced. Furthermore,. . .

L8 ANSWER 10 OF 16 MEDLINE on STN DUPLICATE 6
TI Fas/Fas ligand interaction regulates cytotoxicity of CD4+ T cells against staphylococcal enterotoxin B-pulsed endothelial cells.
PY 1997
SO Biochemical and biophysical research communications, (1997 Oct 29) 239 (3) 782-8.
Journal code: 0372516. ISSN: 0006-291X.
AB . . . by endothelial cells, in inducing endothelial cell apoptosis. The human endothelial cell line, EA.hy926 cells, was cultured with or without **interferon**-gamma (IFN-gamma) and further incubated with CD4+ T cells in the presence or absence of SEB. After this cocultivation, the cytotoxicity. . . EA.hy926 cells with augmented HLA-DR and -DQ expression, this cytotoxicity was more significant. The addition of anti-HLA-DR and -DQ monoclonal **antibodies** (mAbs) or human Fas **chimeric** protein (hFas-**Fc**) reduced the cytotoxicity. FasL expression was induced in CD4+ T cells cocultured with SEB-pulsed EA.hy926 cells, especially when the EA.hy926. . .

L8 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 7
TI Intercellular adhesion molecule-3 is the predominant co-stimulatory ligand for leukocyte function antigen-1 on human blood dendritic cells.
PY 1995
SO European journal of immunology, (1995 Sep) 25 (9) 2528-32.
Journal code: 1273201. ISSN: 0014-2980.
AB . . . the DC. Although blood and tonsil DC express ICAM-1 (CD54) and ICAM-2 (CD102) on their surface, anti-ICAM-1 and anti-ICAM-2 monoclonal **antibodies** (mAb) have little inhibitory activity on the DC-stimulated mixed leukocyte reaction (MLR). We therefore examined the expression of the more. . . blood DC expressed significantly more ICAM-3 than ICAM-1 or ICAM-2 as assessed by flow cytometry. Treatment of resting DC with **interferon**-gamma led to increased expression of ICAM-1; however, ICAM-2 and ICAM-3 levels remained relatively constant. Solid-phase recombinant **chimeric** molecules ICAM-1-, ICAM-2- and ICAM-3-**Fc** were able to co-stimulate CD4+ T lymphocyte proliferation in conjunction with suboptimal solid-phase CD3 mAb 64.1. However, the anti-ICAM-3 mAb. . .

L8 ANSWER 12 OF 16 MEDLINE on STN DUPLICATE 8
TI The extended hinge region of IgG3 is not required for high phagocytic capacity mediated by Fc gamma receptors, but the heavy chains must be disulfide bonded.
PY 1993
SO European journal of immunology, (1993 Jul) 23 (7) 1546-51.
Journal code: 1273201. ISSN: 0014-2980.
AB **Fc** gamma receptor (**Fc** gamma R) phagocytosis and respiratory burst were induced by **chimeric** mouse-human anti-(4-hydroxy-5-iodo-3-nitrophenyl) acetyl IgG3 **antibodies** with mutations in hinge and/or in CH1 region. IgG3 mutants with different hinge length ranging from 47 to 0 amino. . . high activity, while the IgG3/IgG4 hybrids revealed a slightly reduced activity. However, the hingeless (0-h) mutant was negative, except after **interferon** -gamma stimulation when it became slightly positive. Interestingly, HM-1 was as active as the IgG3 mutants. With polymorphonuclear leucocytes (PMN) as. . . to that of the IgG3 mutants. The phagocytic activity of

U937 was inhibited by monomeric IgG, indicating the importance of **Fc** gamma RI. In contrast, with PMN both blockage of **Fc** gamma RII and cleavage of **Fc** gamma RIII were required to significantly reduce the phagocytosis and respiratory burst, thus showing that both receptors contribute to the. . .

L8 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
TI Colony-stimulating factor enhancement of myeloid effector cell cytotoxicity towards neuroectodermal tumor cells
PY 1993
SO British Journal of Haematology (1993), 83(4), 545-63
CODEN: BJHEAL; ISSN: 0007-1048
AB Expts. were conducted to determine the optimal conditions for colony-stimulating factor-enhanced neutrophil- and mononuclear phagocyte-mediated **antibody**-dependent cell-mediated cytotoxicity (ADCC) using monoclonal **antibodies** to disialogangliosides expressed on neuroectodermal tumor target cells. Neutrophil ADCC was most effective at effector:target ratios of 100:1, with maximal. . . factor (G-CSF) were the most potent stimulators of neutrophil ADCC, and enhanced ADCC activity was inhibited in the presence of **antibody** to **Fc** receptor type II (FcRII). GM-CSF and macrophage colony-stimulating factor (M-CSF) treatment of freshly isolated monocytes inhibited **antibody**-independent cytotoxicity but enhanced **antibody**-dependent responses. After 3 days in culture with CSF, 3-10-fold enhancement of ADCC against melanoma target cells was observed at effector:target. . . ADCC was obtained when GM-CSF, M-CSF, or interleukin 3 (IL-3) were used in conjunction with a secondary stimulus. Although γ **interferon** (γ-IFN) did not augment the cytotoxic capability of GM-CSF- and IL-3-stimulated macrophages, prominent cytotoxic enhancement was seen when M-CSF-stimulated macrophages were exposed to γ-IFN. A **chimeric** mouse/human monoclonal **antibody** was found to be equivalent in activity to the murine **antibody** in neutrophil ADCC; however, in macrophage ADCC assays with submaximal effector cell stimulation, the **chimeric** **antibody** was associated with a 2-fold greater response. Thus, under specific conditions, CSFs capable of increasing the number and functional activity of mature myeloid effector cells enhance **antibody** -dependent cytotoxicity to neuroectodermal tumor target cells.

L8 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
TI Mapping and comparison of the interaction sites on the Fc region of IgG responsible for triggering antibody dependent cellular cytotoxicity (ADCC) through different types of human Fcγ receptor
PY 1992
SO Molecular Immunology (1992), 29(5), 633-9
CODEN: MOIMD5; ISSN: 0161-5890
AB In the present study 3-iodo-4-hydroxy-5-nitrophenacetyl (NIP)-specific **antibodies** were compared for induction of **antibody** dependent lysis (ADCC) of NIP-derivatized red blood cells effected by pre-stimulated U937 or HL-60 cells and by killer (K) cells. **Chimeric antibodies** were used having heavy chains corresponding to human IgG subclasses 1-4, and including site-directed mutants of IgG3 as well as the aglycosylated form of IgG3; a mouse IgG2b **antibody** and a site-directed mutant IgG2b were also examined Recombinant **interferon** (rIFN)-stimulated U937 or HL-60 cells express increased levels of **Fc**γRI compared to unstimulated cells; PMA stimulated HL-60 and U937 cells to express an increased level of **Fc**γRII compared to unstimulated cells; K cells expressed **Fc**γRIII. Using these effector cell populations and the target cells mentioned above, anti-NIP **antibodies** were compared with different heavy chain constant domains for their ability to induce ADCC through human **Fc**γRI, **Fc**γRII and **Fc**γRIII. The results suggest that all three human **Fc**γ receptors appear to recognize a binding site on IgG within the lower hinge (residues 234-237) and trigger ADCC via this. . .

L8 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
TI Anti-Rh(D) heteroantibodies and pharmaceutical composition containing same

for drug targeting and therapy using macrophages
PY 1991
1991
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
AB **Chimeric antibodies** comprise all or part of anti-Rh(D) blood-group substance **antibody** linked with all or part of an **antibody** to a receptor for **Fc** fragment of Igs that is not blocked by IgG. These **chimeric antibodies** are bound to erythrocytes encapsulating, e.g. macrophage activators, antiinfective agents, and anticancer agents, via the Rh(D) surface antigen on the erythrocytes, and the complexes target macrophages and are thus useful in therapies involving macrophages. The F(ab')2 fragment of monoclonal **antibody** H2D5D2 (anti D) was coupled to the FAb' fragment of monoclonal **antibody** 32.2 (anti **Fc** γRI). This **chimeric antibody** was reacted with Rh-pos. erythrocytes loaded with γ **interferon**. U937 tumor cells were inhibited using human macrophages and the complex.

L8 ANSWER 16 OF 16 MEDLINE on STN
TI Augmentation of tumor antigen expression by recombinant human interferons: enhanced targeting of monoclonal antibodies to carcinomas.
PY 1990
SO Cancer treatment and research, (1990) 51 413-32. Ref: 59
Journal code: 8008541. ISSN: 0927-3042.
AB . . . standpoint, studies using the intact IgG have shown that, in a majority of patients injected with IgG, human anti-mouse IgG **antibodies** develop that hamper the effectiveness of subsequent **antibody** administration. It is believed that the human anti-mouse **antibody** response is directed against the **Fc** region of the IgG molecule. The elimination of this region through fractionation of the Mab to obtain the minimum binding. . . the genes encoding for individual Mabs, reduce them via restriction endonuclease techniques, and insert human immunoglobulin constant regions. The resulting **chimeric antibodies** are believed to reduce the development of human anti-mouse **antibodies**. Effective Mab therapy of human tumor lesions may also be achieved through the recruitment of a portion of the host's. . . An example is the use of anti-idiotype Mabs that use as immunogen a Mab to a tumor antigen. The anti-idiotype **antibodies** are selected for binding to the antigen binding, or idiotype, region of the first Mab. The binding sites of the new anti-idiotype Mabs should reflect the 'internal image' of the original antigen. The anti-idiotype **antibodies** may be used to immunize patients (i.e., vaccines) in an attempt to mount an active immune response against the antigen-positive tumor cells. Recent studies have shown a synergism between **interferon**-alpha and an anti-idiotype Mab for the in-vivo antitumor activity in a murine B-cell lymphoma experimental model. Whether an **interferon**-mediated increase in the tumor antigen or the **Fc** receptor was part of the synergism was not investigated. Mabs alone have also been shown to elicit cytotoxic activity in vitro and tumoricidal activity in vivo. **Antibodies** of the IgG2a isotype can direct macrophage-mediated cytotoxicity. These studies revealed the importance of the number of **antibody** sites per cell as well as the number of cells that bind the IgG2a Mab, thus suggesting a 'threshold' requirement. . .